

February 16, 1973

Dr. Olen Kew
Department of Microbiology
University of Washington
Seattle, Washington 98105

Dear Dr. Kew,

I have your phone message about neolactose. This was discussed in the 1951 Cold Spring Harbor Symposium and again in the volume "Genetics in the 20th Century" edited by L.C. Dunn. I discussed the possible significance of constitutive mutants in a debate with Jacques Monod which appears in the discussion of "Enzymes, Units of Biological Structure and Function" edited by O.H. Gabbler, Academic Press 1956. At that time the Pasteur group believed that the inducer functioned as a kind of template that played an instructive role in enzyme specificity; they tried to counter the implications of the constitutive mutation by postulating that this behavior was the consequence of the synthesis of an internal inducer. My counter-argument against that was that lactase constitutive cells were not induced with respect to the galactose pathway as would be the case with every then known galactoside. Not long after that the PaJaMo experiment experiment broke through all our intellectual blinders and repressors were born.

You asked why I did not refer to this any further? I guess I have to ask why some of my contemporaries, who are well aware of this work, did not undertake that discussion. I felt I had certainly fulfilled my responsibility in bringing the facts on to the table. I would have pursued the issue further if I had gone more deeply into the structure of beta-galactosidase, so as to be able to verify the identity of the enzyme produced in the constitutive compared to the induced cells. Other matters -- especially the working out of transduction and the application of this technique to the immunogenetics of *Salmonella* -- preoccupied me more during this period.

Kenneth Schaffner of the Department of Philosophy, University of Pittsburgh, has written a very perceptive history of this area of scientific discovery. He may still not get have sent his manuscript to the journal and I suspect he would be interested in any comment you wished to add to his account.

Sincerely yours,

Joshua Lederberg
Professor of Genetics

JL/rr

Kew, Olen